



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,032	02/05/2004	Frank D. Lee	EPT-001C2	5991
51414 7590 06/16/2008 GOODWIN PROCTER LLP PATENT ADMINISTRATOR EXCHANGE PLACE BOSTON, MA 02109-2881				
EXAMINER LIN, JERRY				
ART UNIT 1631		PAPER NUMBER		
NOTIFICATION DATE 06/16/2008		DELIVERY MODE ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PatentBos@goodwinprocter.com
hmcpeake@goodwinprocter.com
glenn.williams@goodwinprocter.com

Office Action Summary

Application No.

10/773,032

Applicant(s)

LEE ET AL.

Examiner

JERRY LIN

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-8, 13, 19-21, 23, 24, 26-28, 30-34, 42 and 44-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-8, 13, 19-21, 23, 24, 26-28, 30-34, 42 and 44-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 February 2008 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-846)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicants' arguments and amendments, filed February 11, 2008, have been fully considered and they are deemed to be persuasive. The combination of references previously cited does not teach the newly recited limitation of an amino acid sequence encoded by RNA spanning a splice junction. However, newly cited Hongo et al. is relied upon in the rejections below to teach this limitation, therefore the arguments are moot in view of the new grounds of rejection. The following rejections are newly applied as necessitated by amendment. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1-4, 6-8, 13, 19-21, 23, 24, 26-28, 30-34, 42, and 44-47 are under examination.

Drawings

2. The petition for color drawings filed under 37 CFR 1.84(a) has been granted. Please see the attachment.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

Art Unit: 1631

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 3-4, 19, 24, 26, 28, 30-34, 42, 44, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dours-Zimmermann et al. (The Journal of Biological Chemistry (1994) Volume 269, Number 52, pages 32992-32998) in view of Hongo et al. (Journal of General Virology (1994) Volume 75, pages 3503-3510) in view of Jemmerson (Proc. Natl. Acad. Sci. (1987) Volume 84, pages 9180-9184) in view of Arenkov et al. (Analytical Biochemistry (2000) Volume 278, pages 123-131).

The instant methods are drawn to a method of detecting and quantifying target proteins in a sample by fragmenting proteins in a sample, exposing the fragmented proteins to an addressable array of capture agents, wherein the capture agent binds to a PET that comprises the amino acid sequence encoded by the RNA spanning a splice junction and using a secondary capture agent labeled with a detectable moiety to detect a captured fragment.

Regarding claims 1, 30, and 42, Dours-Zimmermann et al. teach a method of fragmenting proteins using a predetermined proteolytic protocol (page 32993, left column bottom) wherein the protein fragments contain epitopes that are unambiguously indicative of the presence of a sample of the target proteins and comprise the amino acid sequence encoded by the RNA with a splice junction (page 32995); creating antibodies (capture agents) that selectively interact with the epitopes (page 32995) and contacting the antibodies with the protein fragments (page 32995) to detect the presence or absence of the target proteins (page 32995).

However, Dours-Zimmermann et al. do not teach wherein the amino acid sequence encoded by the RNA spans the splice junction.

Hongo et al. disclose synthesizing unspliced and spliced mRNAs from the same segment of RNA that contains a splice junction and translating those mRNAs to yield proteins (abstract; page 3503, left column). Furthermore, Hongo et al. teach detecting polypeptides encoded by mRNA using a molecular assay (abstract).

However, neither Dours-Zimmermann et al. do nor Hongo et al. teach wherein the proteins are denatured.

Regarding claims 1, 30, and 42, Jemmerson teaches creating peptide fragments by a denaturation and proteolytic process (page 9180, right column-page 9181, left column); creating antibodies specific for the peptide fragments, and using the created antibodies to detect the peptide fragments in an assay (page 9181, left column; page 9182, right column).

However, Dours-Zimmermann, Hongo et al. and Jemerson do not teach presenting the antibodies (i.e., capture agents) in an array format.

Regarding claims 1, 30, and 42, Arenkov et al. teach presenting antibodies in an array format and using a secondary capture agent to detect the target protein (abstract; page 126, right column – page 127, left column, top); wherein the secondary capture agent labeled with a fluorophore binds to an epitope separate from the solvent accessible binding surfaces (abstract; page 126, right column – page 127, left column, top).

Regarding claims 3-4, 24, 33, 34, and 46, Arenkov et al. teach wherein the capture agent is an antibody or a non-antibody (page 126); wherein the secondary capture agent labeled with a fluorophore binds to an epitope separate from the solvent accessible binding surfaces (abstract; page 126, right column – page 127, left column, top).

Regarding claim 26, Dours-Zimmermann teaches extracting the target proteins from whole cell lysate, which would include a billion molar excess of unrelated proteins or fragments relative to the target protein (page 32993, left column bottom).

Regarding claims 19 and 28, Dours-Zimmermann teaches wherein the cells are grown in an artificial environment (page 32993, left column, under “Cell Cultures”); and where the target protein may be a biomarker for a splice variant (abstract).

Regarding claims 31-32, Arenkov et al. teach wherein the solid support is disposed in a manner that encodes the identity of the capture agents (i.e., an

Art Unit: 1631

addressable array) (abstract); wherein there are 2-100 or more different capture agents (abstract; page 125, left column bottom).

Regarding claim 44, Arenkov et al. teach wherein the array of capture agents interacts with different epitopes (page 126).

All the elements of the instant claimed method and instant claimed array are known in the references by Dours-Zimmermann et al., Hongo et al., Jemmerson, and Arenkov et al. Each of the references teach methods of detecting a polypeptide or protein of interest. The only difference between the claimed invention and the recited reference is that the claimed invention is the combination of these old elements into a single method or array. Furthermore, one of ordinary skill in the art would have the reasonable expectation that the combination of these teachings would allow the detection of a protein or peptide fragment translated from an RNA spanning a splice junction. Thus, it would have been obvious to one of ordinary skill in the art to combine the methods of Dours-Zimmermann et al., Hongo et al., Jemmerson, and Arenkov et al., because the method taught by each reference is not dependent on the other methods, and the combination of the methods may be performed to achieve predictable results of detecting the presence or absence of proteins encoded by RNA spanning a splice junction.

This rejection is necessitated by amendment.

5. Claims 2, 6-8, 13, 20, 21, 23, 26, 27, 45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dours-Zimmermann et al. (The Journal of

Art Unit: 1631

Biological Chemistry (1994) Volume 269, Number 52, pages 32992-32998) in view of Hongo et al. (Journal of General Virology (1994) Volume 75, pages 3503-3510) in view of Jemmerson (Proc. Natl. Acad. Sci. (1987) Volume 84, pages 9180-9184) in view of Arenkov et al. (Analytical Biochemistry (2000) Volume 278, pages 123-131) as applied to claims 1, 3-4, 19, 24, 28, 30-34, 42, 44, and 46 above, and further in view of Wagner et al. (US 6,897,073 B2).

The instant methods are drawn to a method of detecting and quantifying target proteins in a sample by fragmenting proteins in a sample, exposing the fragmented proteins to an addressable array of capture agents, wherein the capture agent binds to a PET that comprises the amino acid sequence encoded by the RNA spanning a splice junction and using a secondary capture agent labeled with a detectable moiety to detect a captured fragment.

Dours-Zimmermann et al., Hongo et al, Jemmerson, and Arenkov et al. are applied as above.

However, neither Dours-Zimmermann et al., Hongo et al., Jemmerson, nor Arenkov et al. teaches determining the amount of target protein in the sample by averaging the results obtained from each said capture agent.

Regarding claims 2, 20, 21, and 45, Wagner et al. also teach a method of detecting proteins using arrays of protein-capture agents (abstract) which includes contacting the array with cleaved or denatured protein analytes (membrane bound proteins) from body fluids (column 35, lines 22-44) and quantifying the amount of a target protein by averaging the result (including if the total amount of the detected

Art Unit: 1631

proteins is averaged by one spot in the array) (column 35, line 63-column 36, line 23; column 39, lines 12-50).

Regarding claims 6 and 47, Wagner et al. teach arrays with capture agents bind to the same PET (column 12, line 14 - column 13, line 30); furthermore, Wagner et al. teach finding proteins that bind to the same PET at different affinities (column 30, line 54 – column 34, line 45).

Regarding claims 7 and 8, Wagner et al. teach using cellular extracts which would contain multiple forms of protein such as pro-form or mature form proteins (column 35, lines 22-44).

Regarding claims 13, Wagner et al. teach detecting protein fragments (processed forms) of cellular extracts and determining the ratio of one form of protein to another form (column 45, lines 32-39; column 38, lines 43-65).

Regarding claim 23, Wagner et al. teach wherein a secondary capture agent may be used for detection using fluorescent methods (column 36, lines 24-57).

Regarding claim 27, Wagner et al. teach wherein the PET is identified based on a sequenced genome (column 30, lines 42-54).

All the elements of the instant claimed method and instant claimed array are known in the references by Dours-Zimmermann et al., Hongo et al., Jemmerson, Arenkov et al., Wagner et al. Each of the references teaches methods of detecting a polypeptide or protein of interest. The only difference between the claimed invention and the recited reference is that the claimed invention is the combination of these old elements into a single method or array. Furthermore, one of ordinary skill in the art

Art Unit: 1631

would have the reasonable expectation that the combination of these teachings would allow the detection of a protein or peptide fragment translated from an RNA spanning a splice junction. Thus, it would have been obvious to one of ordinary skill in the art to combine the methods of Dours-Zimmermann et al., Hongo et al., Jemmerson, Arenkov et al., and Wagner et al., because the method taught by each reference is not dependent on the other methods, and the combination of the methods may be performed to achieve predictable results of detecting the presence or absence of encoded by RNA spanning a splice junction. .

This rejection is necessitated by amendment.

Withdrawn Rejections

6. Applicant's arguments and amendments, filed February 11, 2008, with respect to the rejections made under 35 U.S.C. §112 and 103 in the previous office action have been fully considered and are persuasive. The amendments were sufficient to overcome the rejection made under 35 U.S.C. §112. Furthermore, the references of Dours-Zimmermann et al., Jemmerson, Arenkov et al., and Wagner et al. used in the rejection made under 35 U.S.C. §103 do not teach the limitation of RNA spanning a splice junction. These rejections have been withdrawn.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

Art Unit: 1631

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JERRY LIN whose telephone number is (571)272-2561. The examiner can normally be reached on 7:00-5:30pm, M-TH.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1631

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. L./

Examiner, Art Unit 1631

/Marjorie Moran/

Supervisory Patent Examiner, Art Unit 1631